

REMARKS

This in reply to the Office Action mailed 5 August 2009. By this Amendment claims 1, 31 and 37-39 have been amended. New claims 40 - 41 have been added.

Interview Summary

The applicant thanks the Examiner for the courtesy of the telephonic interviews extended to the applicant's agent on 16 December 2009, 6 January 2010 and 22 January 2010 respecting this application and related continuation-in-part application serial No. 12/102,669. During such interviews the Examiner indicated that the presently pending claims might be allowable if the applicant amended the independent claims to indicate that the receptor was an aptamer. The Examiner indicated that she had reconsidered the cited art and would not maintain the rejection under 35 USC § 103(a) based on the art of record. The Examiner and the applicant's agents reviewed the working examples in the application showing reduction to practice of embodiments of the invention, including the examples set forth in the drawings. The active step recited in claim 1 occurring upon binding of an analyte to the sensor was discussed.

35 USC § 112

In reply to the Examiner's rejection of claims 1-4, 6-13, 15-23, 25-27 and 29-39 under 35 USC § 112, first paragraph, the Examiner is respectfully requested to withdraw this rejection in view of the following comments. In the following comments paragraph numbers refer to the specification as published.

It is submitted that the applicant has set forth in the specification sufficiently detailed, relevant identifying characteristics of the invention such that a person skilled in the art would recognize that the applicant was in possession of the claimed subject matter. For example, the features recited in claim 1 are described, *inter alia*, at paragraphs 10 and 52-55; Figures 1-2 and the Example commencing at paragraph 91. More particularly, the applicant describes an analyte sensor comprising a first oligonucleotide stem (e.g. a first DNA strand); a second oligonucleotide stem (e.g. a second DNA strand); and a receptor capable of binding analyte (e.g. a high affinity DNA aptamer for detecting the presence of the analyte adenosine). As indicated at paragraph 92 of applicant's specification, NMR studies have confirmed that this aptamer, upon binding two

molecules of adenosine, undergoes an adaptive folding forming a tightly hydrogen-bonded and stacked helical structure. Further, applicant's Example at paragraph 109 of the specification clearly demonstrates that the adenosine-induced folded structure of the aptamer receptor was capable of facilitating charge transfer between the first and second oligonucleotide stems, as recited in claim 1. It is therefore submitted that all of the features of claim 1 are clearly described in applicant's specification.

The guidelines set forth in MPEP § 2163 state that the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant identifying characteristics, i.e. structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. As indicated above, the applicant has described an actual reduction to practice of both an integrated-ligand sensor as illustrated, *inter alia*, in Figure 1(b), and Example 2.3.1 and a coupled-ligand sensor as illustrated, *inter alia*, in Figure 1(a), 15(a) and Example 2.3.2. It is submitted that a person skilled in the art would recognize from the applicant's specification, for example at paragraph 114, that the functionality of the coupled-ligand sensor does not depend on the conductivity of the aptamer domain and that there is only a requirement for a conformational change in the receptor upon binding of analyte.

The applicant's specification also describes, for example at paragraph 6, that it is well-known in the art that *in vitro* selection methods are capable of generating a wide variety of aptamer sequences capable of specifically binding a large number of different analytes, including molecular species which do not normally interact with DNA or RNA. Further, a person skilled in the art would recognize that such aptamers are capable of undergoing a conformational change upon binding a cognate ligand analyte. Figure 10 of applicant's specification describes a process for *in vitro* selection of sensors specific for a particular target analyte. The Stanton et al. and Breaker et al. references cited by the Examiner, which are discussed further below, describe other means for constructing molecular switches comprising nucleic acids which undergo a conformational change upon binding of an effector.

The specification also describes that it is well-known in the prior art that naturally occurring and aptamer binding sites may be made exclusively of RNA. At paragraph 67 of the specification, the applicant describes how the invention may be employed to identify RNA-binding analytes such as the small HIV-coded proteins Tat and Rev, which bind specifically to respective RNA sites in HIV genomic RNA. As described by the applicant, the binding of the analytes results in a conformation change, namely an induced-fit folding of the RNA loops.

The applicant's specification clearly describes how the oligonucleotide stems may be formed from DNA, RNA, DNA/RNA composites and other oligonucleotide constructs including nucleic acid analogues and nucleic acid-like molecules capable of base pairing. It is submitted that such different embodiments would be readily apparent to a person skilled in the art, especially having regard to the prior art literature described in the specification at paragraph 81 and incorporated by reference. Further, as stated in the guidelines set forth in MPEP § 2163, information which is well-known in the art need not be described in detail in the specification.

It is submitted that the guidelines set forth in MPEP § 2163 require that the Examiner consider each claim separately. On pages 4 and 10 of the Office Action the Examiner has stated generally that the claims are drawn to various listed features without identifying what features correspond with what claims. Although the Examiner has not addressed each of the applicant's claims separately, it is submitted the written description requirement has been satisfied in respect of each of the claims in issue, including claims directed to particular species, such as claim 29 which specifically relates to an adenosine analyte.

It follows from the foregoing that it would be readily apparent to a person skilled in the art that the applicant was in possession of the subject matter of the claims, including the claimed genus and species, as of the application filing date. The applicant notes that no objections have been made in the corresponding European application that the claimed subject matter was not adequately described. Given these submissions and the strong presumption that an adequate written description of the claimed invention is present when the application is filed, the Examiner is respectfully requested to withdraw the rejection under 35 USC § 112.

In reply to the Examiner's reference to extracts from the specification at pages 5-7 of the Office Action, it is submitted that the specification describes techniques to optimize sensitivity of signal

detection, for example to alter signal to noise ratios. It is submitted that it would be apparent to a person skilled in the art that such optimization does not affect the operability of the invention and that the applicant was in possession of the claimed subject matter.

35 USC § 103(a)

In reply to the Examiner's rejection of claims 1-4, 6-13, 15-23, 25-27 and 29-39 under 35 USC § 103(a), the Examiner is respectfully requested to reconsider this rejection in view of the following comments.

The Examiner has asserted that the above claims are unpatentable over Stanton et al. (US 2003/0087239) and Breaker (Current Opinion in Biotech., Vol. 13, pages 31-39, 2002) in view of the combined teachings of Meade et al. (USPN 6,238,870), Berner et al. (USPN 6,144,869), and Gasper et al. (J. Am. Chem. Soc., Vol. 119, pages 12,762-12,771, 1997).

Stanton et al., as understood, relates to a target activated nucleic acid sensor which results in a change in the optical qualities of the sensor rather than a change in the electrical properties and the charge transfer characteristics. The sensor includes an optical signaling unit which changes its optical properties upon allosteric modulation of the sensor.

Breaker, as understood, relates to RNA and DNA molecules engineered solely to function as enzymes. The engineered molecular switches trigger catalytic events when a target molecule becomes bound. The molecules may be arranged in an RNA array. Breaker does not relate to changes in the transfer of electrical charge. Binding of analyte is detected by means of radioactive labelling (e.g. Figure 5).

Meade et al., as understood, relates to nucleic acid mediated electron transfer, wherein the nucleic acid comprises a covalently attached electron transfer moiety. The moiety is preferably a transition metal complex attached to a single stranded nucleic acid. The construct may be used as a new form of gene probe. Meade et al. does not relate to the sensing of a broad spectrum of analytes resulting from a conformational change when the analyte binds to a specific receptor site as described in applicant's specification.

Berner et al. relates to monitoring of physiological analytes. The analytes are extracted transdermally from a biological system, for example to measure blood glucose levels. Berner et al., as understood, does not comprise an electronic sensor system comprising oligonucleotide stems operatively coupled to a receptor site.

Gasper et al., as understood, relates to a finding that oxidative damage may migrate in double stranded DNA. A series of duplex DNA structures were prepared that incorporate an anthraquinone group. DNA damage at a location distal from the anthraquinone group following irradiation is due to migration of a radical cation through the duplex DNA. This feature, including a reference to the Gasper et al. reference and the fact that not all perturbations to the helix prevent charge transfer, is referred to at paragraph 3 of the applicant's specification. Gasper et al. does not relate to the sensing of analytes.

The Examiner states that Stanton et al. describes a biosensor that "elicits a detectable signal" when it switches from one conformation state to a second conformational state upon binding of an analyte. As mentioned above, Stanton et al. relates to optical signaling and does not disclose a sensor as recited in applicant's claims where a change in charge transfer results upon analyte binding.

The Examiner states that Breaker "elicits a detectable signal" when the sensor switches from one conformational state to another conformational state. As mentioned above, Breaker also does not relate to changes in the transfer of electrical charge upon binding of analyte. Binding of analyte is detected by means of the release of a cleaved, and radioactively labeled, RNA substrate.

The Examiner has acknowledged that neither Stanton et al. and nor Breaker teach a sensor which switches from a conformational state which impedes charge transfer to a conformational state where charge transfer is permitted. More particularly, it is submitted that neither of these references disclose a sensor as claimed by the applicant having a structure where a receptor is operatively connected to first and second oligonucleotide stems to effect changes in charge transfer upon binding of an analyte to a receptor.

It is submitted that none of the Meade et al., Berner et al. and Gasper et al. references remedy the deficiencies of Stanton et al. and Breaker. As indicated above, Meade et al. relates to a single

stranded nucleic acid having a covalently attached electron transfer moiety. Meade et al. does not describe a specific receptor site operatively coupled to first and second oligonucleotide stems and is not adapted to detect a wide variety of different analytes. Berner et al. also does not describe an analyte sensor coupled to first and second oligonucleotide stems. The electrode design of Berner et al., as shown in Figure 4, is of an entirely different type and scale than the applicant's invention and does not relate whatsoever to nucleotide and nucleic acid conductivity. As indicated above, Gasper et al. is referred to as general background art in applicant's specification and does not relate to the sensing of analytes.

It is submitted that there is no teaching, suggestion or motivation in either Stanton et al. or Breaker that any advantage would be achieved by detecting binding of analyte electronically, and particularly by means of a receptor operatively connected to first and second oligonucleotide stems. It is therefore submitted that neither Stanton et al. nor Breaker would look to Meade et al., Berner et al. or Gasper et al. for guidance in modifying their sensors. Moreover, it is submitted that even if such references were combined, they would not result in the subject matter of applicant's claims for the reasons set out above. None of the prior art teach or suggest the idea of connecting a receptor site to oligonucleotide stems in such a manner that binding of analyte to the receptor causes a detectable change in charge transfer between the stems due to a change in conformation of the sensor.

In view of the above submissions, and the Examiner's comments in the telephonic interview of 22 January 2010 noted above, the Examiner is respectfully requested to withdraw the rejection of claims 1-4, 6-13, 15-23, 25-27 and 29-39 under 35 USC § 103(a).

Double Patenting

In reply to the Examiner's provisional obviousness-type double patenting objection at pages 15-16 of the Office Action, the applicant acknowledges that copending Application No. 12/102,669 is a continuation-in-part of the present application and is currently under examination. No conflicting claims have been patented.

Sequence Compliance Notice

Applicant has amended the Specification at pages 8 and 9 to provide SEQ ID NOs. for Figures 12 and 15 and has inserted a Sequence Listing on a new page of the Specification.

As required by 37 CFR 1.821(f) and 1.821(g), the content of the sequence listing information recorded in computer-readable form is identical to the written (on paper) sequence listing and includes no new matter.


A copy of the Notice to Comply accompanies this Amendment.

Summary

In summary, it is submitted that the Applicant's claims under examination and the newly asserted claims are patentable over the cited references alone or in combination. Accordingly, the Applicant respectfully requests withdrawal of the rejections and allowance of this application. If the Examiner has any questions about this paper, or is not convinced that the claims are in condition for allowance, Applicant requests a personal interview with the Examiner.

Respectfully submitted,

By:



Donald B. Haslett

Reg. No. 28,855

tel: 503-227-5631

fax: 503-228-4373

e-mail: don@chernofflaw.com

Portland, Oregon
USA